**PATENT** 

## **DOCKET NO.: ISIS-2112**

On page 7, in line 20, delete "prefereably" and substitute --preferably-- therefor.

On page 7, in line 24, delete "ineteger" and substitute --integer-- therefor.

On page 13, in line 34, delete "deravative" and substitute –derivative-- therefor.

On page 13, in line 35, delete "deravative" and substitute –derivative-- therefor.

## In the claims:

In line 4 of claim 7, delete "ineteger" and substitute -integer-- therefor.

## Remarks

Claims 1-36 are pending in this application. The specification and claims have been amended to correct editorial errors. No new matter has been added.

Claims 1-6 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. The Office Action appears to assert that the specification does not provide enablement for the preparation of polymers of claim 1 other than those of claim 21, or "similar" polymers. Applicants respectfully request reconsideration, as those of skill in the art would be able to make and use the claimed compounds.

As Applicants stated in their prior response, the use of protective groups in organic chemistry, and the use of protective groups in peptide chemistry in particular, is especially well developed, as exemplified by the Greene and Wuts reference ("Greene"), cited by Applicants.

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The Office Action appears to acknowledge this, but appears to assert that the art is well developed only as "directed to protection of reactive groups that will permit the synthesis of amide or peptide bonds while protecting carboxyl and or amino moieties on subunits as defined in instant claims 21 etc." Office Action at p. 3. However, Applicants respectfully point out that neither the Greene text, nor the general knowledge in the art, is so limited. To the extent that the Office Action intends to assert that some difference exists in terms of protective groups strategies employed for nucleobases vs. amino groups or carboxyl groups, Applicants respectfully point out that Greene's teaching is not limited to protective groups used for carboxyl or amino groups at the exclusion of protective groups for nucleobases. Indeed, the Greene text is an extensive compendium of protecting group methodologies for use not merely in peptide chemistry, but for all areas of synthetic Organic Chemistry, and includes protecting groups and procedures for protection of hydroxyl groups (including phenols and catechols), carbonyl groups, carboxyl groups, thiol groups, and amino groups. In addition, the art is replete with teachings of protecting strategies for nucleobases during oligonucleotide synthesis. Moreover, the present specification contains extensive exemplification of synthesis using protected nucleobases. Applicants therefore respectfully assert that those of skill in the art would encounter no difficulty in preparing the compounds of claims 1-6, and request reconsideration and withdrawal of this rejection.

Claims 1-6 and 21, 22, and 24 are rejected under § 102 as allegedly being anticipated by Summerton *et al.* The Office Action has maintained its assertion that Summerton et al.

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anticipates the present claims, apparently on the basis that the benzyol or nitrobenzoyl protecting groups used in the Summerton et al. reference are "aromatic lipophilic molecules" as recited in the definition of "conjugates" the present claims. However, Applicants respectfully point out that the Summerton benzyol and nitrobenzoyl groups cited by the Office Action are protecting groups, i.e., labile moieties that are appended temporarily to protect functional groups during assembly of the Summerton et al. oligomers, and which are removed prior to the completion of the Summerton et al. oligomers. In contrast, the "aromatic lipophilic molecule" conjugate groups of Applicants' claimed compounds are not "protecting groups" that are removed, but rather are a component of the complete PNA conjugate. The Summerton et al. reference neither discloses nor suggests such conjugates in a completed PNA oligomer, instead merely mentioning the species cited by the Office Action as possible temporary protecting groups for use in the preparation of non-conjugate oligomers. Because the Summerton et al. reference does not anticipate the present claims, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 28 of U.S. Pat. Application serial number 08/595,387, now U.S. Patent No. 5,773,571, issued June 30, 1998. Applicants will address this rejection upon indication of allowable subject matter in the present application.

Claims 21, 22, 24, 30, 31 and 32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8 and 34-48 of

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U.S. Pat. Application serial number 08/468,719. Applicants will address this rejection upon indication of allowable subject matter in the present application.

In view of the foregoing, Applicants submit that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is earnestly solicited.

Respectfully submitted,

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